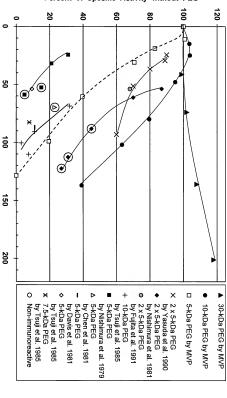


Figure 1A: Retention of Activity by PEGylated Candida Uricase

Percent of Specific Activity without PEG



Mass of PEG Coupled (kDa) / Uricase Subunit

Figure 1B: Retention of Activity by PEGylated Candida Uricase

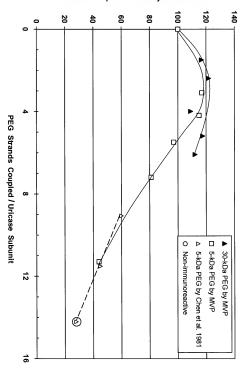


Figure 2A: Retention of Activity by PEGylated Porcine Uricase

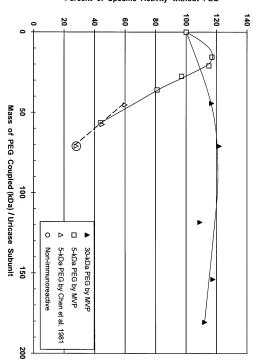


Figure 2B: Retention of Activity by PEGylated Porcine Uricase

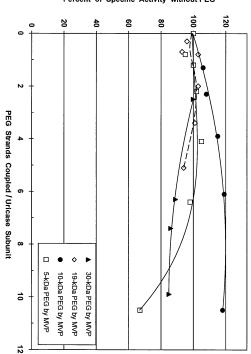


Figure 3A: Retention of Activity by PEGylated Pig-Baboon Chimeric Uricase



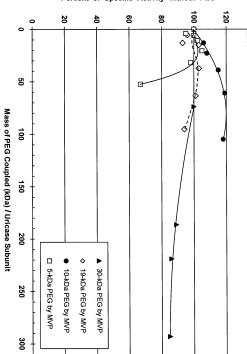
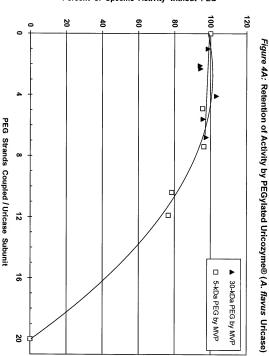
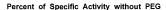


Figure 3B: Retention of Activity by PEGylated Pig-Baboon Chimeric Uricase

Percent of Specific Activity without PEG





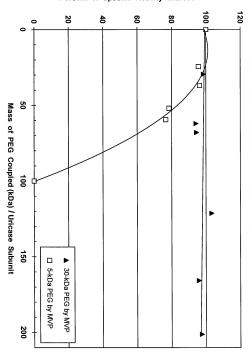


Figure 4B: Retention of Activity by PEGylated Uricozyme® (A. flavus Uricase)

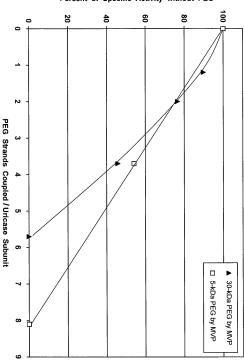


Figure 5A: Retention of Activity by PEGylated Soybean Uricase



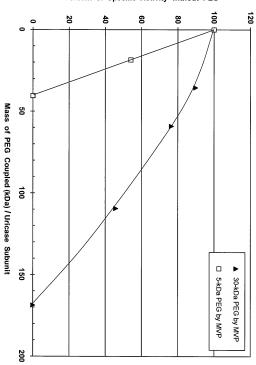


Figure 5B: Retention of Activity by PEGylated Soybean Uricase

Figure 6: Deduced amino acid sequences of Pig-Baboon Chimeric (PBC) uricase, PBC uricase that is truncated at the amino and carboxyl terminals (PBC-NT-CT) and Porcine uricase containing the mutations R291K and T301S (PKS uricase), compared with the porcine sequence (SEQ ID NO: 1) and the baboon sequence (SEQ ID NO: 2).

| PORCINE MAHYRNDYKK NDEVEFVERG YCKDMIKVLH IQRDGKYHSI 40 | | | | | |
|---|-----------|--------------------------------|------------------------------|---------------------|-----|
| PBC-NT-CT | Porcine | MAHYRNDYKK NDEVEFVRTG | YGKDMIKVLH | IQRDGKYHSI | 40 |
| PKS | PBC | porcine sequence 1-225 | \rightarrow | | 40 |
| PKS | PBC-NT-CT | porcine sequence | 1-219 → | | 34 |
| Baboon | PKS | | | | 40 |
| PBC | Baboon | | | IQRDGKYHSI | 40 |
| PBC-NT-CT | Porcine | KEVATSVOLT LSSKKDYLHG | DNSDVIPTDT | IKNTVNVLAK | 80 |
| PKS | PBC | porcine sequence → | | | 80 |
| Baboon KEVATSVQLT LSSKKDYLHG | PBC-NT-CT | porcine sequence → | | | 74 |
| Procine | | | | | |
| PBC | | | DNSDIIPTDT | IKNTV H VLAK | |
| PBC-NT-CT | | FKGIKSIETF AVTICEHFLS | SFKHVIRAQV | YVEEVPWKRF | |
| PKS | | | | | |
| Baboon | | | | | |
| Porcine | | | | | |
| PBC PBC-NT-CT POrcine sequence → porcine seq | | | | | |
| PBC-NT-CT | | | CEVEQIRNGP | PVIHSGIKDL | |
| PKS | | | | | |
| Baboon | PBC-NT-CT | porcine sequence \rightarrow | | | |
| Porcine | | | | | |
| PBC | Baboon | EKNGVKHVHA FIHTPTGTHF | CEVEQ L R S GP | PVIHSGIKDL | 160 |
| PBC-NT-CT | Porcine | KVLKTTQSGF EGFIKDQFTT | LPEVKDRCFA | TQVYCKWRYH | |
| PKS | PBC | porcine sequence \rightarrow | | | 200 |
| Baboon KVLKTTQSGF EGFIKDQFTT LPEVKDRCFA TQVYCKWRYH 200 | PBC-NT-CT | porcine sequence → | | | |
| Porcine OGRDVDFEAT WDTVRSIVLQ KFAGPYDKGE YSPSVQKTLY 240 Dorcine sequence PSC NT CT Daboon sequence PSC Daboon sequence POCCINE | PKS | porcine sequence → | | | |
| PBC Porcine sequence → ← baboon sequence 240 | Baboon | KVLKTTQSGF EGFIKDQFTT | LPEVKDRCFA | TQVYCKWRYH | 200 |
| PBC-NT-CT | Porcine | QGRDVDFEAT WDTVRSIVLQ | KFAGPYDKGE | YSPSVQKTLY | |
| PKS | PBC | porcine sequence | → ← bal | oon sequence | |
| Baboon QCRDVDFEAT WGTIRDLVLE KFAGPYDKGE YSPSVQKTLY 240 | PBC-NT-CT | porcine sequence | → ← bal | oon sequence | 234 |
| Porcine | PKS | porcine sequence → | | | |
| PBC | Baboon | QCRDVDFEAT WGTIRDLVLE | KFAGPYDKGE | YSPSVQKTLY | |
| PBC-NT-CT | Porcine | DIQVLTLGQV PEIEDMEISL | PNIHYLNIDM | SKMGLINKEE | 280 |
| PKS | | baboon sequence → | | | |
| Baboon DIQVLSLSRV PETEDMEISL PNIHYFNIDM SKMGLINKEE 280 Porcine VLLPLDNPYG RITGTVKRKL TSRL 304 PBC baboon sequence → 295 PKS porcine ← baboon → 304 → 304 | | baboon sequence → | | | |
| Porcine | | | | | |
| PBC baboon sequence → 304 PBC-NT-CT baboon sequence → 295 PKS porcine ← baboon → 304 | Baboon | DIQVLSLSRV PEIEDMEISL | PNIHY F NIDM | SKMGLINKEE | 280 |
| PBC-NT-CT baboon sequence \rightarrow 295 PKS porcine \leftarrow baboon \rightarrow 304 | Porcine | VLLPLDNPYG RITGTVKRKL | | | |
| PKS porcine ← baboon → 304 | PBC | baboon sequence → | 304 | | |
| 1 Carrett / Land | PBC-NT-CT | baboon sequence → | 295 | | |
| Baboon VLLPLDNPYG KITGTVKRKL SSRL 304 | PKS | porcine ← baboon | → 304 | | |
| | Baboon | VLLPLDNPYG KITGTVKRKL | SSRL 304 | | |

Relative Serum Uricase Activity

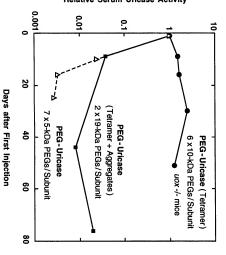


Figure 7: Serum Uricase Activity 24 Hours after Each PEG-Uricase Injection, Relative to the First Injection

REPLACEMENT SHEET

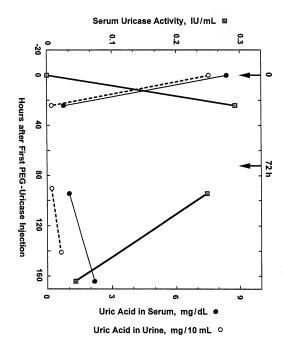
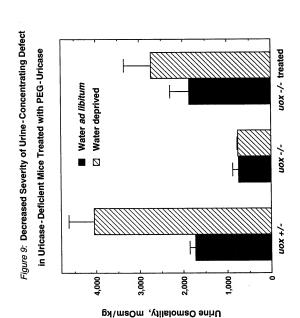
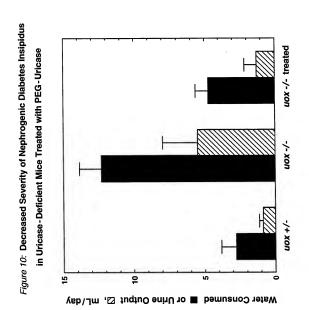


Figure 8: Inverse Relationship between Serum PEG-Uricase Activity and Uric Acid Levels in the Serum and Urine of a Uricase-Deficient Mouse



REPLACEMENT SHEET

Appl. No. 09/839,946 Amendment Dated: September 18, 2007 Reply to Decision on Appeal of: July 18, 2007 SKGF Ref No.: 2057.0090003/BJD/SAC



Appl. No. 09/839,946 Amendment Dated: September 18, 200 Reply to Decision on Appeal of: July 18, 2007 SKGF Ref No.: 2057.0090003/BJD/SAC REPLACEMENT SHEET

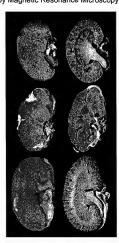
Figure 11:

Decreased Severity of Uric Acid-Induced Nephropathy after Treatment with PEG-Uricase, as Visualized by Magnetic Resonance Microscopy

Kidney of normal mouse

Kidney of untreated uricase knockout mouse

Kidney of PEG-uricase treated uricase knockout mouse



Surface Coronal Rendered Slice